

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/004216

International filing date (day/month/year)
05.10.2004

Priority date (day/month/year)
10.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4365, A61P35/00

Applicant
VERNALIS (CAMBRIDGE) LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004216

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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Box No. II Priority

1. ☐ The following document has not been furnished:
- ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).
- Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-14 (in part)

because:

- ☒ the said international application, or the said claims Nos. 12-14 (I.A. only) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-12 (in part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004216

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|----------|
| Novelty (N) | Yes: Claims | |
| | No: Claims | 1-15 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-15 |
| Industrial applicability (IA) | Yes: Claims | 1-11, 15 |
| | No: Claims | 12-14 |

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 12-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The reference to a mechanism, the "inhibition of HSP90" (second medical use claims 1-11 and method of treatment claim 12), is not considered a clear definition of the disease (Clarity, Art. 6 PCT). The medical use claims shall refer to a real, defined therapeutical application, such as those diseases listed in claims 13 and 14.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 2004/054505 A (KOLODZIEJ STEPHEN A ; VERNIER WILLIAM F (US); LEE LEN F (US); PHARMACI) 1 July 2004 (2004-07-01)
- D2: DD 275 688 A (UNIV LEIPZIG) 31 January 1990 (1990-01-31)
- D3: WO 93/13664 A (SCHERING AGROCHEMICALS LTD) 22 July 1993 (1993-07-22)
- D4: SHERIF S M ET AL: "BETA-ENAMINONITRILES IN HETEROCYCLIC SYNTHESIS: A NOVEL ONE-POT SYNTHESIS OF THIOPHENES AND THEIR FUSED DERIVATIVES" JOURNAL OF CHEMICAL RESEARCH. SYNOPSES, LONDON, GB, 1996, pages 356-357, XP001166932 ISSN: 0308-2342
- D5: LEISTNER SIEGFRIED ET AL: "1,3-Bis(pyridin-2-ylthio)propan-2-ones, Bis(thieno(2,-3-b)pyridin-2-yl)ketones and 5H-Bispyrido(3,2':4,5)thieno(2,3-b:2',3'-e)pyridin-11-ones" ARCHIV DER PHARMAZIE (WEINHEIM), vol. 326, no. 12, 1993, pages 959-961, XP009042878 ISSN: 0365-6233
- D6: WO 03/037860 A (KASIBHATLA SRINIVAS RAO ; ZHANG LIN (US); BOEHM MARCUS F (US); FAN JUN) 8 May 2003 (2003-05-08)

Novelty - Article 33(2) PCT

D2 (DD275688) discloses compounds of formula (I) that appear to be of pharmaceutical use (abstract). Although there are no explicit therapeutic indications mentioned in D2, it is considered novelty-destroying for the independent claims (second medical use claim 1, method of treatment claim 12, composition claim 15), having regard to the unclear definition of the claimed therapeutic effect (cf. Item III above).

In D5 (Leistner et al.), compound 3d appears to fall under formula (I). D3

(WO9313664) discloses cyclohexyl 3,6-diamino-5-cyano-4-methylthiothienot2,3-b]pyridine- 2-carboxylate (example 50). Also the publication by Sherif et al. (D4) discloses compounds falling under formula (I).

It should be pointed out that the intended use, "pharmaceutical or veterinary", is not a limiting feature in product claim 15. Hence, any composition of a compound of formula (I) destroys novelty for such a claim.

The disclosure in the above documents is therefore considered novelty-destroying for the subject-matter of claim 15.

Industrial Applicability - Article 33(4) PCT

For the assessment of the present claims 1-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.